Tansley insight

Adaptive introgression: how polyploidy reshapes gene flow landscapes

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Summary

Rare yet accumulating evidence in both plants and animals shows that whole genome duplication (WGD, leading to polyploidy) can break down reproductive barriers, facilitating gene flow between otherwise isolated species. Recent population genomic studies in wild, outcrossing *Arabidopsis arenosa* and *Arabidopsis lyrata* indicate that this WGD-potentiated gene flow can be adaptive and highly specific in response to particular environmental and intracellular challenges. The mechanistic basis of WGD-mediated easing of species barrier strength seems to primarily lie in the relative dosage of each parental genome in the endosperm. While generalisations about polyploids can be fraught, this evidence indicates that the breakdown of these barriers, combined with diploid to polyploid gene flow and gene flow between polyploids, allows some polyploids to act as adaptable 'allelic sponges', enjoying increased potential to respond to challenging environments.

I. Introduction

The origin and history of new species, the net of life, is not a simple bifurcation of new species from common ancestors. Instead, population genomic studies are commonly revealing recurrent, interwoven cycles of separation and admixture (Kearns *et al.*, 2018; He *et al.*, 2019), with an increasing recognition that lineage differentiation occurs in the face of ongoing admixture (i.e. speciation-with-gene-flow; Feder *et al.*, 2012). A source population begins to diversify, but until ultimate divergence is achieved by completed reproductive isolation, populations remain in contact through gene flow (Fig. 1) in a 'grey zone of speciation' (de Queiroz, 2007). Even when populations have differentiated to such an extent that they colonise distinct distribution ranges, gene flow may re-emerge in the form of hybridisation after secondary contact. The intensity of such gene flow depends on both extrinsic and intrinsic factors. One such intrinsic factor now receives revived attention with the benefit of population genomics: whole genome duplication (WGD) (Marburger *et al.*, 2019; Novikova *et al.*, 2020), first noted by Stebbins (1956) and Harlan & de Wet (1963).
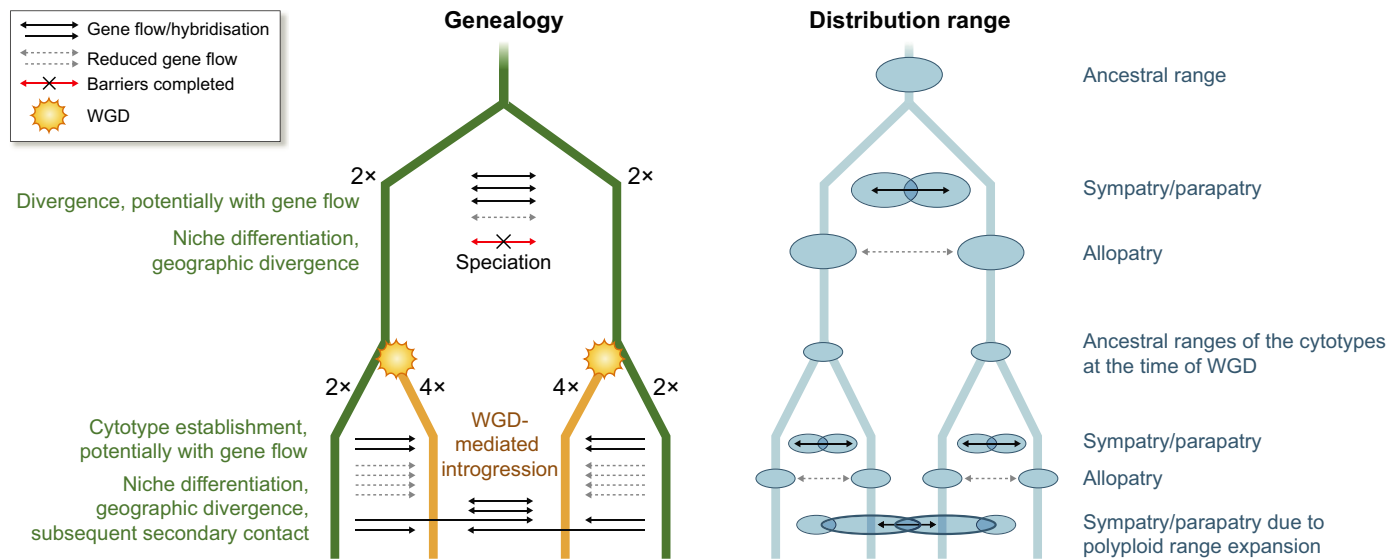
Fig. 1 Schematic autopolyploid speciation of two species and two cytotypes, diploids (2×) and autotetraploids (4×). Genealogy and distribution ranges at the various stages of speciation and cytotype differentiation are shown. Note that this is a simplification of the speciation process: each cytotype can differentiate into various lineages, and polyploidisation could eventually occur multiple times, polytopically. Also for simplification, homoploid hybridisation between diploids is not shown. Arrows indicate the type of bi- or unidirectional gene flow at the different speciation stages: gene flow, and, respectively, hybridisation, reduced gene flow, and complete reproductive isolation. WGD, whole genome duplication.

A large effect mutation, WGD leads to genomic instabilities, especially when coupled with hybridisation. These can include epigenetic shock, perturbed gene expression, imbalanced cytonuclear interactions, and meiotic instability (De Storme & Mason, 2014), with direct negative consequences on fertility. Despite these challenges, there is growing evidence that WGD may facilitate introgressive hybridisation ('introgression' hereafter), thereby representing a potential engine of diversification (Marburger *et al.*, 2019; Novikova *et al.*, 2020). On occasion, introgression provides a source of novel variation that transfers traits of adaptive value (adaptive introgression, 'the transfer by introgression of relatively small genomic regions from a donor species that have positive fitness consequences in the recipient species' (Suarez-Gonzalez *et al.*, 2018)). Here we explore this interplay between WGD and adaptive introgression, focussing on recent population genomic works that have enabled high-resolution views. We first summarize studies that give evidence for WGD-mediated adaptive gene flow, followed by addressing the mechanistic bases and population genomic effects of WGD that promote gene flow.

II. WGD can mediate adaptive gene flow

Effects of WGD are often idiosyncratic. Thus, it is no surprise that WGD may either facilitate the establishment of gene flow barriers in the speciation grey zone (Husband & Sabara, 2004) or not, depending on the species and ploidy level (Sutherland & Galloway, 2017). Whatever the pace of barrier formation, however, the derived lineages commonly occupy a distinct niche and geography relative to progenitors (Fig. 1). In cases of secondary contact between cytotypes (incomplete isolation), hybridisation may then allow transfer of traits with adaptive benefits. Such adaptive gene flow can occur between different

ploidies (overwhelmingly from diploid to tetraploid, via unreduced gametes) within a single species (Baduel *et al.*, 2018; Monnahan *et al.*, 2019), or among close relatives (Schmickl & Koch, 2011; Marburger *et al.*, 2019; Novikova *et al.*, 2020), often in a cytotype-specific manner.

Stebbins (1956) was the first to outline WGD-mediated gene flow within the polyploid complex *Dactylis glomerata*, based on cytotaxonomics. In the *D. glomerata* complex the diploid species/subspecies differ from each other in appearance, habitat and geographic distribution, but nonetheless are easily intercrossed to produce mainly fertile and vigorous hybrids. In contrast to the diploids, the tetraploid is widely distributed and highly variable. According to Stebbins, the tetraploid is likely to be of allopolyploid origin, although autopolyploidy cannot be ruled out (Lumaret *et al.*, 1989). As a result of its spread, it is thought that the tetraploid came into contact with additional diploids and hybridised with them, acquiring genes from them in the process.

Recent genomic studies focusing on autopolyploids give clear examples where ploidy increases may potentiate hybridisation (Schmickl & Koch, 2011; Baduel *et al.*, 2018; Marburger *et al.*, 2019; Monnahan *et al.*, 2019; Novikova *et al.*, 2020). Crucially, these works cleanly isolate the effects of WGD from hybridisation, as they treat within-species WGDs (*auto*polyploids, not *allo*polyploids, which confound WGD with hybridisation). In these cases, diploid cytotypes are fully isolated, but gene flow is established between cytotypes through WGD. We use the term 'WGD-mediated gene flow' in cases where WGD potentiates gene flow which does not occur at the diploid level, that is, between diploids that are reproductively isolated from each other (representing different lineages or species).

While there is highly provocative parallel evidence in a diploid/polyploid frog system (Novikova *et al.*, 2020), the most detailed

genomic evidence of WGD-mediated gene flow of adaptive alleles comes from plants, namely two wild outcrossing members of the genus *Arabidopsis*. Whereas in *Arabidopsis arenosa* WGD facilitates introgression due to secondary contact between a geographically expanding tetraploid and ecogeographically isolated diploid lineages (Molina-Henao & Hopkins, 2019; Monnahan *et al.*, 2019), WGD potentiates hybridisation between *A. arenosa* and *Arabidopsis lyrata* (Arnold *et al.*, 2016; Marburger *et al.*, 2019) by overcoming the strong postzygotic isolation barrier present between the two species at the diploid level (Lafon-Placette *et al.*, 2017). In *A. arenosa*, asymmetric introgression of alleles of the flowering time regulator *CONSTANS* from diploids to tetraploids contributed to adaptation to disturbed habitats by facilitating rapid cycling (Baduel *et al.*, 2018).

For *A. arenosa* and *A. lyrata*, demographic modelling supported bidirectional gene flow between the tetraploids of these species, and obvious signatures of gene flow and extreme selection coincided at discrete genes (Marburger *et al.*, 2019). Whole genome duplication-facilitated introgression could be narrowed down to single gene-sized selective sweeps directly overlapping alleles important for both extreme edaphic (serpentine) adaptation in tetraploids as well as the rapid evolution of greater meiotic fidelity, changed levels of endopolyploidy, and possible changes in overall transcriptional regulation post-WGD (Arnold *et al.*, 2016; Marburger *et al.*, 2019; Seear *et al*, 2019).

III. Mechanistic basis for WGD-mediated hybridisation

Ecological niche differentiation and geographic separation of cytotypes (Husband & Schemske, 2000; Ramsey, 2011) are increasingly well supported as being broadly important for polyploid establishment. This is borne out, for example, by cases of higher rates of climatic niche evolution in polyploids compared to their diploid progenitors (Baniaga *et al.*, 2020). Perhaps surprisingly, even this initial barrier to gene flow can end up laying a foundation for introgression, because niche expansion (i.e. expansion of niche breadth) can increase the chance of secondary contact with polyploids from sister species. Evidence from polyploid complexes (e.g. López-Jurado *et al.*, 2019) supports the notion that tetraploids in particular show high rates of niche expansion compared to their diploid progenitors. Coupled with a WGD-induced boost of clonality (Van Drunen & Husband, 2019) and resultant increased yet context-dependent colonization potential (Pyšek & Richardson, 2007), niche expansion may increase the likelihood of secondary contact between formerly isolated species.

Contact can promote hybridisation if coupled with a WGD-induced breakdown of postzygotic, endosperm-based incompatibility. In the endosperm, the paternal genome promotes endosperm growth while the maternal genome represses it (Fort *et al.*, 2016) in a dosage-sensitive, 'effective ploidy' manner, with a strict requirement of a 2 : 1 maternal to paternal ratio (Povilus *et al.*, 2018). This ratio of effective ploidy between the parental genomes must be balanced in order to allow for viable seed formation, and this balance, the 'endosperm balance number' (EBN), whose molecular basis has been proposed to be the number and expression

level of paternally expressed genes (Lafon-Placette *et al.*, 2018), eventually reaches a species-specific optimum (Johnston & Hanneman, 1982). Due to different EBNs in hybridising species, the endosperm of interspecific hybrids usually shows developmental defects. According to the EBN hypothesis, the effective ploidy in the endosperm increases with the ploidy of the species. For example, increasing the ploidy of a low EBN species matches its effective ploidy with a higher EBN species, thus allowing production of viable hybrid seeds (Johnston & Hanneman, 1982). Both in *Solanum*, *Arabidopsis* and *Capsella*, homoploid hybrid seeds are very often inviable due to endosperm problems; however, either natural or artificial polyploidisation of one parental species is sufficient to restore the viability of hybrid seeds and normal endosperm development (Johnston & Hanneman, 1982; Lafon-Placette *et al.*, 2017, 2018).

IV. Population genomic outcomes of WGD

Accumulating empirical evidence across kingdoms shows how some polyploids can exhibit increased adaptive potential in particular environments (e.g. auto- and allopolyploid *Saccharomyces cerevisiae* (Selmecki *et al.*, 2015; Peris *et al.*, 2020); autopolyploid *Achillea borealis* (Ramsey, 2011); *A. arenosa* (Baduel *et al.*, 2018; Monnahan *et al.*, 2019)). We suggest that on balance this is not because polyploids are generally 'better', but because their very genesis allows for increased organismal diversity over alternate scenarios where diploids exist alone. Polyploids thus represent 'second chances' to achieve different, possibly additional fitness optima.

Many changes that occur upon WGD may underpin these 'second chances', many of which are purely genetic, the most simple being the increase in nucleotide diversity per individual that can occur with increasing ploidy, after an initial bottleneck. Modelling in concert with evolution experiments in challenging media showed higher rates of beneficial mutations in tetraploid yeast strains compared to their (initially isogenic) haploid and diploid progenitors (Selmecki *et al.*, 2015). Young polyploids may also occasionally benefit from relaxed purifying selection on potentially deleterious – but occasionally beneficial – recessive mutations. Compared to a rather subtle effect for nonsynonymous single nucleotide polymorphisms (SNPs) (Monnahan *et al.*, 2019), this effect is strong for transposable elements (TEs), which are frequently major effect alleles. Relaxed purifying selection on TE insertions can result in increased TE load after WGD, with over-accumulation at environmentally responsive genes, such as the major flowering-time repressor *FLC* in *A. arenosa* (Baduel *et al.*, 2019). The increase in allelic diversity and, thus, adaptive potential for tetraploids seems to be linked with challenging environments in *A. arenosa*, similar to yeast: it is the rapid-cycling, heat- and drought-associated ruderal lineage that seems particularly prone to accumulating adaptive potential (Baduel *et al.*, 2018, 2019).

While indeed some introgressed variation is retained (especially in autopolyploids, which mask increased levels of genetic load), most is certainly purged (Martin & Jiggins, 2017). Purging of maladaptive variants can be driven by various classes of incompatibilities, and the strength of this is dependent on a combination of

recombination rate, drift (Martin *et al.*, 2019) and, possibly, ploidy (Kulmuni & Pamilo, 2014). In genomic regions with higher recombination rates, foreign chromosomal linkages that enter a population through hybridisation break down more rapidly, which will separate clusters of foreign deleterious alleles, hence weakening selection against introgression. In the case of adaptive variants, recombination rates can be lowered due to structural variants in large, possibly introgressed haplotypes, in which these variants are clustered (Todesco *et al.*, 2020). If polyploids engage in introgression, an increased effective recombination rate of higher ploidies (Pecinka *et al.*, 2011; although note a sometimes lower crossover rate, e.g. Bomblies *et al.*, 2016 and references therein) can promote introgression, although the possible link between polyploidy and recombination rate remains to be demonstrated. Genetic drift, too, influences the introgression landscape, by driving hybrid incompatibilities to high frequencies, but also in this case polyploidy promotes introgression, because of reduced genetic drift (Ronfort *et al.*, 1998). Importantly, when considering the effect of WGD on the adaptive value of introgression, the timing of introgression must be taken into account. Much of the selection against introgression may occur in the early hybrid generations (Harris & Nielsen, 2016), and in the case of introgression between polyploids, deleterious incompatibility alleles tend to be masked via dosage and (potentially fixed) heterozygosity in newly formed polyploids (Otto, 2007). As genetic variants of donor species have already been tested by natural selection most often in the donor itself or a closely related genome, they should be less likely to induce negative pleiotropic or epistatic effects in the recipient. This may have been the case in adaptation to WGD itself, which appears to be primarily the adjustment of the meiotic machinery to the challenges of increased ploidy: in the case of *A. lyrata/A. arenosa*, the older tetraploid *A. arenosa* introgressed a greater number of candidate beneficial alleles into the younger tetraploid *A. lyrata* than vice versa (Marburger *et al.*, 2019).

V. Conclusion

Taken together, the emerging genomic evidence supports the hypothesis that polyploids may be prone to act as 'allelic sponges' (or 'compilospecies' in the words of Harlan & de Wet, 1963), increasing their genetic diversity not only through ongoing gene flow from conspecific diploids, but also with tetraploids with different genomic constitutions due to relaxed barriers to gene exchange at the tetraploid level. These weakened barriers, coupled with population genomic effects of WGD, allow an increased chance of adaptive introgression. Based on these factors, we suggest that polyploids are, therefore, prone to represent diverse and adaptable evolutionary amalgamates, especially in heterogeneous, stressful environments (Wei *et al.*, 2019; Yao *et al.*, 2019).

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